

The rejection does not clearly identify any specific motivation to combine the references and further states no teaching or suggestion that would cause the ordinary practitioner to combine the two references. Accordingly, the rejection is defective. Indeed, it is believed that the combination of references is most definitely hindsight based and should properly be withdrawn.

(iii) The Reference Teaches A Separation Step

Finally, Applicants wish to point out that the reference teaches the operation of a separations step. At column 13 under the heading: "Noise is Washed Away" the reference reads: "Next, the unbound probe is washed away from the cells by one wash step using a solution of 0.1 x SSC (1x SSC = 0.15M NaCl and 0.015 M sodium citrate, pH 7.4) with 0.1% Triton X-100<sub>TM</sub>. Applicants position that Bresser et al. teach a separation step is further supported by Examples 2-12 wherein in each case a post hybridization wash step or pelleting step is performed prior to detection of the stained cells.

Taken together these statements by Bresser et al. demonstrate that a separation step is most definitely contemplated and even necessary in all of their embodiments. As discussed previously, Yurov et al. most definitely teach that a wash (a separation step) is to be performed after fixation. Consequently, these references alone and in combination simply do not teach the absence of a separations step to remove either or both of fixative agents and/or excess probe. Moreover, Bresser et al. is more appropriately viewed as a **teaching away** from the presently claimed subject matter. Accordingly, there is no reasonable expectation of achieving the presently claimed subject matter and therefore the rejection should be withdrawn.

(iv) Argument Conclusion

For at least these reasons, it is respectfully submitted that the present rejection of claims 2, 4, 8 and 21 based upon the combination of Yurov et al. with Bresser et al. is improper under 35 U.S.C. § 103(a) and should be withdrawn.

E. *The Rejection Based Upon Yurov et al. and Ortiz et al.*

(i) Statement Of The Rejection

At paragraph 5 of the Office Action dated November 19, 2003, the Examiner rejected claims 13, 19 and 20 as being unpatentable over Yurov et al. in view of Ortiz et al. (Molecular and Cellular Probes (1998) 12: 219-226). The Examiner relies upon arguments made in paragraph 1 of the Office Action with respect to the Yurov et al. reference, the accuracy of which Applicants dispute. The Examiner appears to take the position that Yurov et al. does not teach various elements/limitations of the rejected claims but takes the position that Ortiz et al. teach these elements/limitations.

(ii) The Rejection Is Defective

The rejection does not clearly identify any specific motivation to combine the references and further states no teaching or suggestion that would cause the ordinary practitioner to combine the two references. Accordingly, the rejection is defective. Indeed, it is believed that the combination of references is most definitely hindsight based and should properly be withdrawn.

(iii) The References Teach Non Analogous Art

The combination of these references by the Examiner is most curious since Ortiz et al. does not teach or even suggest the application of their probes to an in-situ hybridization assay. Moreover, the primary reference, Yurov et al., does not teach the application of a self-indicating probe. Accordingly, it is respectfully submitted that the two references are non-analogous art and are therefore improperly combined especially given the lack of common subject matter and/or relevant suggestion or teaching. For these reasons it is clear that there simply is no reasonable expectation of successfully combining these references to achieve the presently claimed subject matter. Accordingly, it is believed that the rejection should be withdrawn.

(iv) Argument Conclusion

For at least these reasons, it is respectfully submitted that the present rejection of claims 13, 19 and 20 based upon the combination of Yurov et al. with Ortiz et al. is improper under 35 U.S.C. § 103(a) and should be withdrawn.

*F. The Rejection Based Upon Yurov et al. and Iris et al.*

(i) Statement Of The Rejection

At paragraph 6 of the Office Action dated November 19, 2003, the Examiner rejected claim 15 as being unpatenable over Yurov et al. in view of Iris et al. (US 6,403,309). The Examiner relies upon arguments made in paragraph 1 of the Office Action with respect to the Yurov et al. reference, the accuracy of which Applicants dispute. The Examiner appears to take the position that Yurov et al. does not teach various elements/limitations of the rejected claims but takes the position that Iris et al. teach these elements/limitations.

(ii) The Rejection Is Defective

The rejection does not clearly identify any specific motivation to combine the references and further states no teaching or suggestion that would cause the ordinary practitioner to combine the two references. Accordingly, the rejection is defective. Indeed, it is believed that the combination of references is most definitely hindsight based and should properly be withdrawn.

(iii) The References Teach Non Analogous Art

The combination of these references by the Examiner is most curious since Iris et al. does not teach or even suggest the application of their probes to an in-situ hybridization assay. Moreover, the primary reference, Yurov et al., does not teach the application of "anti-probes" to "mop-up" excess probe in an in-situ assay. Accordingly, it is respectfully submitted that the two references are non-analogous art and are therefore improperly combined especially given the lack of common subject matter and/or relevant suggestion or teaching. For these reasons it is clear that there simply is no reasonable expectation of successfully combining these references to achieve the presently claimed subject matter. Accordingly, it is believed that the rejection should be withdrawn.

(iv) Argument Conclusion

For at least these reasons, it is respectfully submitted that the present rejection of claim 5 based upon the combination of Yurov et al. with Iris et al. is improper under 35 U.S.C. § 103(a) and should be withdrawn.

G. *The Rejection Based Upon Yurov et al. and Hyldig-Nielsen et al.*

(i) Statement Of The Rejection

At paragraph 7 of the Office Action dated November 19, 2003, the Examiner rejected claims 11, 12 and 17 as being unpatentable over Yurov et al. in view of Hyldig-Nielsen et al. (US Published Application US 2001/0010910). The Examiner relies upon arguments made in paragraph 1 of the Office Action with respect to the Yurov et al. reference, the accuracy of which Applicants dispute. The Examiner appears to take the position that Yurov et al. does not teach various elements/limitations of the rejected claims but takes the position that Hyldig-Nielsen et al. teach these elements/limitations.

(ii) The Rejection Is Defective

The rejection does not clearly identify any specific motivation to combine the references and further states no teaching or suggestion that would cause the ordinary practitioner to combine the two references. Accordingly, the rejection is defective and should be withdrawn. Indeed, it is believed that the combination of references is most definitely hindsight based and should properly be withdrawn.

(iii) Argument Conclusion

For at least these reasons, it is respectfully submitted that the present rejection of claim 5 based upon the combination of Yurov et al. with Hyldig-Nielsen et al. is improper under 35 U.S.C. § 103(a) and should be withdrawn.

V. SUMMARY

It is believed that this response addresses all rejections set forth in the present Office Action and the application is in ready condition for allowance. In consideration of the preceding remarks, Applicants hereby respectfully request reconsideration of all

pending claims, the withdrawal of all rejections set forth in the present Office Action and issue of a Notice of Allowance by The Office.

#### VI. INTERVIEW

If the Examiner believes a telephonic or personal interview would advance the prosecution of the subject application, the Examiner is invited to contact attorney Gildea during business hours at the telephone or facsimile numbers listed below.

#### VII. FEES

The petition under 37 C.F.R. §1.136(a) that accompanies this paper includes an authorization to deduct the appropriate fee from Deposit Account 02-3240. A Notice of Appeal and associated authorization to deduct the appropriate fee from Deposit Account No 02-3240 also accompanies this paper. No additional fees are believed due The Office for consideration of this paper. If however, The Office determines that any other fee is due, authorization is hereby granted to charge any required fee associated with the filing or proper consideration of this paper to Deposit Account 02-3240.

#### VIII. CORRESPONDENCE/CUSTOMER NUMBER

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IF NOT ALREADY DONE, PLEASE MATCH THIS CASE WITH CUSTOMER NUMBER

**23544**

Respectfully submitted  
on behalf of Applicants,

April 30, 2014

Date

Brian D. Gildea

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Reg. No. 39,995